of HBeAg-positive carrier mothers. J Pediatr Gastroenterol Nutr 1993;17:207-10.

11. Kao JH, Chen PJ, Chen W, Hsiang SC, Lai MY, Chen DS. Amplification of GB virus C/hepatitis G virus RNA with primers from different regions of the viral genome. J Med Virol 1997;51:284-9.

12. Lin HH, Kao JH, Chen PJ, Chen DS. Reply to : Mother-to-infant transmission of hepatitis C virus and breast-feeding. J Pediatr 1995;127:670-1.

13. Lin HH, Kao JH, Hsu HY, et al. Possible role of high-titer maternal viremia in perinatal transmission of hepatitis C virus. J Infect Dis 1994;169:638-41.

Table. Hepatitis G virus in the sera and colostra of HGV-infected mothers

Patient No.	Maternal serum	HGV-RNA level, copies/mL*	
		Colostral supernatant#	Colostral precipitate
1	10^4	$<10^4$	-
2	10^4	$<10^4$	-
3	10^4	$<10^4$	-
4	$5x10^4$	$<10^4$	-
5	$5x10^8$	$<10^4$	-
6	$5x10^4$	$<10^4$	-
7	10^4	$<10^4$	-
8	$5x10^7$	$<10^4$	-
9	10^5	$<10^4$	-
10	$5x10^4$	$<10^4$	-
11	$5x10^4$	$<10^4$	-
12	10^7	$<10^4$	-
13	10^4	$<10^4$	-
14	10^4	$<10^4$	-
15	10^4	$<10^4$	-

*: HGV-RNA level is detected by competitive RT-PCR.

#: All colostral supernatant shows positive HGV-RNA, but the HGV-RNA level $<10^4$ copies/mL.

ABSTRACT

The role of breast-feeding in perinatal transmission of hepatitis G virus (HGV) was explored in 15 HGV-infected mothers and their infants. The 15 carrier mothers had HGV-RNA levels ranging from 10^4 to $5x10^8$ copies/mL. HGV-RNA was present in colostral samples in much lower levels, but none of the 15 breast-fed infants had evidence of HGV infection for up to 1 year of age. Thus breast-feeding seems safe for their infants.

Keywords: Hepatitis G virus (HGV), mother-to-infant transmission, maternal viremia, breast-feeding

Absence of Infection in Breast-fed Infants Born to Hepatitis G Virus-Infected Mothers

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<Running Title> Colostral HGV-RNA

ABSTRACT

The role of breast-feeding in perinatal transmission of hepatitis G virus (HGV) was explored in 15 HGV-infected mothers and their infants. The 15 carrier mothers had HGV-RNA levels ranging from 10^4 to $5x10^8$ copies/mL. HGV-RNA was present in colostral samples in much lower levels, but none of the 15 breast-fed infants had evidence of HGV infection for up to 1 year of age. Thus breast-feeding seems safe for their infants.

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INTRODUCTION

Perinatal transmission as a route of hepatitis G virus (HGV) infection is well established [1-4], but non-parenteral or inapparent parenteral route of HGV infection is unknown. Investigators have examined body fluids and secretions, including saliva, semen, urine, stool and human milk for the presence of hepatitis C virus- ribonucleic acid (HCV-RNA) [5-9], whose biologic activity is very closely to HGV. However, no data of HGV-RNA from human milk were reported as far as now. This prompted us to study the status of HGV-RNA in the colostrum of HGV carrier mothers, and to explore the possibility of transmission of HGV to their infants by breast-feeding.

MATERIALS AND METHODS

Subjects. Between May 1995 and May 1996, we recruited 15 carrier mothers from among 25 pregnant HGV carriers in our previous study [4], and 3 healthy mothers as control subjects. Mothers were defined as carriers of HGV when serum specimen were positive for viral RNA at least twice within an interval of ≥3 months. Maternal blood, 10 ml, and colostrum, 10 ml, were taken from each subject mother 5 days postpartum. For colostral samples, the yellowish fat in the top layer was removed after centrifugation at 1000 g and 4^0 C for 30 minutes, and the supernatant was collected [9,10]. The precipitate was washed twice with phosphate-buffered saline solution and finally restored to its original volume with the same solution. All the supernatants and precipitates of the colostra and maternal sera were stored at -40^0 C until analysis. Blood samples were collected from the infants at 1, 3, 6, 9 and 12 months of age.

Detection and quantification of serum and colostrum HGV-RNA. Serum and colostrum HGV-RNA was detected by reverse transcription-polymerase chain reaction (RT-PCR) with primers from the 5'-untranslated region of the viral genome as previously described [4,11], and the positive samples were further quantified.

To quantify viral RNA level, a competitive RT-PCR assay was used by mixing one-tenth of sample serum RNA with serial dilutions of competitor HGV-RNA that differs from the RNA of interest by an insertion of 37 base pairs [4]. The mixtures were cotranscribed by random hexamers and coamplified by nested PCRs with the two primers. Both PCRs were done under the same conditions described before [4,11]. This competitive RT-PCR could detect 10^4 RNA copies/mL of specimen.

RESULTS

The HGV-RNA levels from each maternal serum and colstrum are shown in Table. All the 15 HGV-infected mothers had positive HGV-RNA in maternal sera ranging from 10^4 to $5x10^8$ copies/mL by competitive RT-PCR; the three healthy mothers had negative results. In colostral samples, the HGV-RNA were present in the supernatant, but the level was much lower ($<10^4$ copies/mL), whereas the precipitate of colostrum had no HGV-RNA. The HGV-RNA level of the serum did not correlate with that of the corresponding colostrum. Thus the blood-to-colostrum gradient of HGV was estimated to be from 10^{-4} to 10^{-8}.

Of the 15 infants, all were breas-fed for 1 month to 4 months, with a mean duration of 2 months. All infants had no HGV-RNA at the end of the follow-up, and thus apparently were not infected by HGV.

DISCUSSION

This present study is the first report in literature that HGV-RNA could be demonstrated to exist in the colostra of HGV carrier mothers, although the level of colostral HGV-RNA was much low. The blood-to-colostrum gradient of HGV is 10^{-4} to 10^{-8}, and no evident correlation is found between paired maternal serum and colostral samples. In addition, none of the infants fed human milk for up to 4 months had HGV infection by 1 year of age. The observation suggests that breast-feeding need not be discouraged for infants born to HGV carrier mothers. This conclusion may be drawn from the following explanation. First, HGV is a blood-borne virus and its infection through breast-feeding in not effective compared with parenteral routes. Second, the amount of HGV in the colostra is low and it is an enteral route. Third, the integrity of the oral and gastrointestinal mucosa of the infant may effectively preclude HGV infection via the enteral route. Lastly, the small amount of HGV present in the colostrum may be easily inactiveted in the gastrointestinal tract [9,12].

Our previous study has shown that the high-titered maternal viremia and mode of delivery are the determinants as the perinatal transmission of blood-borne viruses, such as HCV and HGV [4,13]. Of our 15 HGV carrier mothers, 3 (Nos. 5,8 and 12) with high-titered HGV viremia but they received elective cesarean delivery and their 3 infants spared from the perinatal HGV transmission despite they had been breast-fed.

We conclude that although HGV-RNA are present in the colostrum of HGV carrier mothers, breast-feeding usually does not cause HGV transmission in their infants and thus should not be discouraged.

ACKNOWLEDGRMENTS

This study was supported from the grant of National Science Council (NSC 88-2314-B-002-384), Executive Yuan, R.O.C. We thank Mrs. Kao-Yi Yeh for her skillful technical assistance.

REFERENCES

1. Feucht HH, Zollner B, Polywka S, Laufs R. Vertical transmission of hepatittis G. Lancet 1999;347:615-6.
2. Lin HH, Kao JH, Chen PJ, Chen DS. Mechanism of vertical transmission of hepatitis G. Lancet 19996;347:1116.
3. Moaven LD, Tennakoon PS, Bowden DS, Locarnini SA. Mother-to-baby transmission of hepatitis G virus. Med J Aust 1999;165:84-5.
4. Lin HH, Kao JH, Yeh KY, et al. Mother-to-infant transmission of GB virus C/hepatitis G virus: the role of high-titered maternal viremia and mode of delivery. J Infect Dis 1998;177:1202-6.
5. Wang JT, Wang TH, Lin JT, Sheu JC, Lin SM, Chen DS. Hepatitis C virus RNA in saliva of patients with posttransfusion hepatitis C infection [Letter]. Lancet 1991;337:48.
6. Ogasawara S, Kage M, Kosai K, Shimamatsu K, Kojiro M. Hepatitis C virus RNA in saliva and breast milk of hepatitis C carrier mothers [Letter]. Lancet 1993;341:561.
7. Hsu HH, Wright TL, Luba D, et al. Failure to detect hepatitis C virus genome in human secretions with the polymerase chain reaction. Hepatology 19991;14:763-7.
8. Fried MW, Shindo M, Fong TL, Fox PC, Hoofnagle JH, DiBisceglie AM. Absence of hepatitis C viral RNA from saliva and semen of patients with chronic hepatitis C. Gastroenterology 1992;102:1306-8.
9. Lin HH, Kao JH, Hsu HY, et al. Absence of infection in breast-fed infants born to hepatitis C virus-infected mothers. J Pediatr 1995;126:589-91.
10. Lin HH, Hsu HY, Chang MH, Chen PJ, Chen DS. Hepatitis B virus in the colostra